Meeting of the
Pharmacy and Therapeutics Committee
October 23, 2006
Draft Minutes

Members Present:
Randy Axelrod, M.D., Chair
Mark Oley, R. Ph., Vice Chair
Gill Abernathy, M.S., R.Ph.
Avtar Dhillon, M.D.
James Reinhard, M.D.
Rachel M. Selby-Penczak, M.D.
Renita Warren, Pharm.D.
Tim Jennings, Pharm.D.
Mariann Johnson, M.D.
Katherine Nichols, M.D.

Absent:
Arthur Garson, M.D.
Roy Beveridge, M.D.
A quorum was present

Guests:
Manikoth Kurup, MD, Member Board of Medical Assistance Services
68 representatives from pharmaceutical companies, providers, advocates, associations, etc.

DMAS Staff:
Patrick Finnerty, Agency Director
Cynthia B. Jones, Chief Deputy Director
Bryan Tomlinson, Director, Division of Health Care Services
Reatha Kay, Counsel to the Board, Office of the Attorney General
Keith Hayashi, R.Ph., Clinical Pharmacist
Katina Goodwyn, Pharmacy Contract Manager
Maryanne Paccione, Information Management Consultant

First Health Services Corporation Staff:
Debbie Moody, R.Ph, Clinical Manager
Donna Johnson, R.Ph, Clinical Manager
Justin Lester, Pharm.D, M.B.A., Rebate Support
Doug Brown, R.Ph, Rebate Support
Doug Davis, Executive Account Director

WELCOME AND INTRODUCTIONS FROM PATRICK FINNERTY, DMAS DIRECTOR

Patrick Finnerty welcomed everyone to meeting and the new meeting space. He thanked the members for all of their hard work on the Committee. He commented on the transition of lives from fee for service to Medicare Part D and stated that 60% of that population now has pharmacy coverage through the Part D program. He reminded the Committee members that while the PDL program now includes a smaller population it is still very important.

Mr. Finnerty announced the resignations of Dr. Eleanor Sue Cantrell and Mark Szalwinski, who both recently resigned because of other professional obligations. He expressed his appreciation for all of their work during their tenure on the P&T Committee. Mr. Finnerty welcomed two new Committee members, Katherine Nichols, M.D. and Tim Jennings, Pharm.D. He noted that the addition of these new members allows the Department to remain compliant with Committee composition requirements with eight physicians and four pharmacists

Mr. Finnerty informed the Committee that Conflict of Interest forms were in their notebooks to be completed and returned to the Department. The forms serve as a conflict of interest statement that allows the members to indicate whether they or any immediate family member has received any financial benefits from any pharmaceutical manufacturer within the previous two years. Financial benefits may include compensation, research project funding, gifts or other items of monetary value. All members completed the statement upon appointment and the Department would like to update these annually given the potential for conflict of interest with the functions of the P&T Committee.

Dr. Axelrod asked about the status of the Medicare Part D clawback payments. Mr. Finnerty stated that it still exceeds the prior payment for recipients' pharmacy claims but that CMS did change the calculation and the sum is lower than what was original projected; down from $35 million to $16 million.

COMMENTS AND WELCOME FROM DR. RANDY AXELROD, CHAIRMAN

Dr. Axelrod introduced and welcomed the two new members of the P&T Committee. Katherine Nichols, M.D. is a physician as well as a pharmacist. Dr. Nichols is the Director of Central Virginia Health District in Lynchburg and pediatrician for Advocates for Children. Tim Jennings, Pharm.D. is a pharmacist and currently the Director of Pharmacy Services for Sentara Healthcare including its hospitals and the health plans.

Dr. Axelrod reiterated the importance of the conflict of interest statements due to Committee members' various interactions and career changes. He asked that the Committee be diligent in completing the conflict of interest forms.

Dr. Axelrod reviewed some of the "ground rules" of the P&T Committee. He reminded the Committee that if they meet with two or more members, even socially, it is considered a Committee meeting and must be disclosed to the public.

Dr. Axelrod also explained that the Committee meeting is divided into two separate, distinct parts. First, the clinical review component, which is all "FOIAble", e.g., subject to the Freedom of Information Act in which the Committee must address publicly. All clinical discussions have take place in a public forum. The second part is the confidential component, which is held in a separate meeting location. United States code allows the Committee to hold this confidential meeting to discuss the pricing. At the confidential part of the meeting, clinical issues and evaluations cannot be discussed at all. A representative from the Office of the Attorney General attends the meetings to ensure that these guidelines are followed.

He noted that the drug class reviews are "FOIAble" and open to the public comments during the meeting and that the Committee receives prior to the meeting. He noted that comments from speakers are limited to 3 minutes, which is monitored by a time clock. He asked that each speaker adhere to the time limit, introduce themselves, and disclose any affiliation with drug companies, manufacturers or distributor.

Dr. Axelrod noted that clinical class reviews would be handled by Gill Abnerathy and Mark Oley. Dr. Axelrod stated that the Vice-Chair position is vacant due to the resignation of Mark Szalwinski and Mark Oley has accepted this position.

Dr. Axelrod reviewed the meeting agenda.

ACCEPTANCE OF MINUTES FROM March 30, 2006 MEETING

Dr. Axelrod asked if there were any corrections, additions or deletions to the minutes from the March 30, 2006 meeting. None was noted and upon request of the Chairman, the Committee voted on a motion to accept the minutes as written. The Committee voted unanimously to approve the minutes as drafted.

PATRICK FINNERTY REVIEWED THE STATUS OF LONG ACTING NARCOTICS PRIOR AUTHORIZATION

Mr. Finnerty reminded the Committee that at the last meeting there was a decision to terminate the remaining automatic prior authorizations for Long-Acting Narcotics on June 30, 2006 and a reduction in the duration of the prior authorizations for narcotics from one year to six months to ensure continuous monitoring of the medical necessity for these drugs. These automatic prior authorizations were provided to recipients who were stabilized on long acting narcotics and/or had certain diagnoses (i.e., cancer) to allow exemption from prior authorization requirements for these drugs.

The month prior to the termination, the prescribers, providers and recipients' were notified of the change. In addition, at that meeting the committee discussed a concern because some claims for Long-Acting Narcotic were being processed with a default Prescriber ID, thus we could not identify the prescribing doctor. Since that meeting, the automatic prior authorizations for Long-Acting Narcotics were terminated on July 1, 2006. Of the original people with automatic PA's, 367 of them have requested new PAs or received a

PA override based on step therapy criteria between July1, 2006 and September 30, 2006. The PAs were used to process approximately 1,150 long acting narcotics claims. In addition, among all claims for long acting narcotic medications only 4% had a default prescriber ID used to process the claim. This is a substantial change in default ID utilization. The P&T Committee's actions helped to correct the default identification number issue. These recipients can still receive PA's for these drugs but they are just not automatic. In addition, the prior authorization review is now occurring on a six month vs. one year time interval. Mr. Finnerty stated that from the Department's standpoint the changes were working very well.

REVIEW OF NEW DRUGS IN PDL PHASE II

Dr. Sandra S. Baucom, Pediatrician, Renaissance Pediatrics, Chesapeake, Virginia discussed the CNS Stimulants/ADHD – Daytrana™

Dr. Baucom stated that she is board certified pediatrician with 23 years of experience. She is also an assistant clinical professor of pediatrics and family/community medicine at Eastern Virginia Medical School. She is a speaker for Shire and only receives honorium for clinical literatures.

Daytrana™ is a Transdermal Patch for ADHD (Attention Deficit Hyperactivity Disorder) approved by the FDA in June 2006. Daytrana™ is a transdermal patch formulation of methylphenidate to be applied once daily for treatment of ADHD. It is approved for children six years and older. The patch is available in strengths of 10mg, 15mg, 20mg and 30mg. The advantages of the patch are: it is not oral, it is discreet, long acting (12 hours length of action),in many cases it eliminates the need for immediate release oral does in the afternoon, lower cost because only one drug instead of two, and has a lower abuse potential. It is a safe and effective treatment for the treatment of ADHD.

Dr. Nichols asked if this was a first line drug and asked about titrations of the product.
Dr. Baucom answered that titration is easier with the patch than with tablets. The doses start with 10mg and look for score results to titrate upward. Titrate weekly looking for a 25% reduction in score results. Titration is continued as needed if no side effects are seen.

Dr. Dhillon asked about bioavailability.
Dr. Baucom answered that it is 1.1 mg per hour of methylphenidate.

Dr. Axelrod said that it was difficult to manage children on sustained release products.
Dr. Baucom answered that there is a rising profile of blood level, as the blood level goes up then the release from the patch decreases. As the blood level decreases the rate of drug release increases. The patch adjusts for the patients' level. This is important for rapid metabolizers. This is more effective and manageable than tablets.

Dr. Axelrod commented on abuse of this class of drugs on college campuses. The abuse potential of this class needs to be considered differently. These are no longer considered "street drugs". Dr. Baucom added that the short acting forms have a greater "street value" than the long acting drugs.

Dr. Axelrod reminded the Committee and attendees that all drugs are still accessible to recipients, even if they are not considered PDL preferred. This is not a closed formulary. A PA may be needed, but the recipient can receive the drug. Dr. Baucom stated that in her opinion it places a barrier to access.

Mark Oley asked if the patch was a first line therapy.
Dr. Baucom noted that no longer does therapy start with short acting medications. The standard of care is to start with long acting medications.

Dr. Nichols clarified that this is a new delivery system not a new drug. If the patch is not on the PDL, it still does not eliminate access to methylphenidate just the delivery system.

The Committee continued with discussion on the treatment of ADHD in the schools today.

Mark Oley reviewed CNS Stimulants/ADHD – Daytrana™
Daytrana™ is the first transdermal patch for ADHD approved by the FDA. It was approved on April 6, 2006. Daytrana™ is a transdermal patch formulation of methylphenidate to be applied once daily for treatment of ADHD (Attention Deficit Hyperactivity Disorder). The patch is available in strengths of 10mg, 15mg, 20mg and 30mg. Noven Pharmaceuticals manufactures it for Shire US, Inc. An FDA Advisory Committee recommended that the patch's label encourage its use as an alternative treatment for children, ages six to twelve years with ADHD, indicating it should be prescribed only if a child were unable to take an oral formulation. The efficacy of Daytrana™ was established in two controlled clinical trials in children aged six to twelve years old with ADHD. Common adverse events seen in clinical trials included decreased appetite, insomnia, nausea, vomiting, weight loss, tics, and affect lability (mood swings).

Daytrana™ combines methylphenidate with Noven's patented DOT Matrix™ transdermal technology. The transdermal delivery system delivers drug directly through the skin into the bloodstream, and is designed to stay on the skin during the normal daily activities of a child, including swimming, exercising, and bathing.

Formulated as a patch, physicians can manage duration of action and potential side effects of Daytrana™ by instructing the patient to wear the patch for a shorter or longer period than the recommended nine hours daily. In clinical trials, wearing a Daytrana™ patch for nine hours provided duration of effect of twelve hours.

Daytrana™ should not be used by children with allergies to methylphenidate or other ingredients in its formulation. The patch should be applied each morning to clean, dry skin; recommendation is to apply to alternating hips which, should be free of any cuts or irritation. Avoid applying external heat to the patch as absorption may be increased. Skin irritation or allergic skin rashes may occur.

Mark Oley motioned that Daytrana™ be PDL eligible.

Tim Jennings asked what makes a drug PDL eligible.

Dr. Axelrod explained that the Committee looks at the class as a whole and answers the following questions: Are all of the drugs in the class comparable? Is a drug in the class superior? Is it a drug that is dangerous that should be excluded completely? If all of the drugs in a class are comparable, then the class is PDL eligible.

Mark Oley motioned that Daytrana™ be PDL eligible.
Dr. Johnson seconded the motion.
The Committee voted unanimously to consider Daytrana® as PDL eligible.

Mark Oley reviewed two generic Macrolides: Azithromycin (Z-max) and Clarithromycin (Biaxin) for consideration of the generic formulations to determine PDL eligibility. There is no change in the products.

Mark Oley motioned that Azithromycin and Clarithromycin be PDL eligible
Dr. Johnson seconded the motion
The committee voted unanimously to consider Azithromycin and Clarithromycin as PDL eligible.

Mark Oley reviewed the new generic ophthalmic antihistamine ketotifen fumerate (Zaditor) for consideration of the generic formulations to determine PDL eligibility. There is no change in the product.

Mark Oley motioned that ketotifen fumerate be PDL eligible.
Dr. Johnson seconded the motion.
The Committee voted unanimously to consider ketotifen fumerate as PDL eligible.

Mark Oley reported on the Board of Pharmacy's initiatives concerning controlled medications

Mark Oley reviewed the current Virginia Board of Pharmacy initiatives for control medications in schedules CII, CIII AND CIV. The Board had a pilot in Southwest Virginia that became statewide on 6/1/06. This initiative mandates that all pharmacies in Virginia report to a central database every two weeks the following information: patient first and last name, street address, state, zip code, date dispensed, quantity of drug dispensed, pharmacy NCPDP number, drug name, NDC, prescriber name and DEA number, birth date and prescription number. Mr. Oley believes this to be an effective and valuable program and that it has heightened the awareness of the problem of abuse with control medications. He deferred to Gill Abernathy who attended the last Board of Pharmacy meeting to provide information on the status of the program. Gill Abernathy reported that it was discussed at the last Board meeting and that the reporting is going well.

PHASE I PDL ANNUAL REVIEW

J. V. (Ian) Nixon, MD, FACC, Professor of Internal Medicine/Cardiology and the Director of Noninvasive Cardiology Services at VCU/MCV discussed HMG CoA Reductase Inhibitors (Statins)

Dr. Nixon is a consultant for Pfizer as well as on the speakers list for many manufacturers. Dr. Nixon referred to his handout. Dr. Nixon presented data on the statin class as it pertains to reducing incidence of stroke in the Medicaid population. He is a co-author on the current guidelines for the prevention of stroke, published in June 2006. His major points were:

- Stroke as part of the overall cardiovascular disease is a burden and accounts for almost 4000 deaths in Virginia per year. The impact on morbidity, productivity and long-term care is profound.
- In his opinion, cholesterol lowering has not been considered a primary strategy in managing stroke risk until recently.
- The data with statins in managing stroke risk provides a framework of benefit in managing stroke in patients at varying degrees of overall cardiovascular risk.
- In his opinion, Lipitor™ has distinguished itself among the category of statins producing rapid, relevant reductions in stroke risk in patients at varying degrees of stroke, including those with a previous stroke. He reviewed the following articles that he believes support his opinion:
    - Primary Prevention of Ischemic Stroke: A Guideline From the American Heart Association/American Stroke Association Stroke Council: Cosponsored by the Atherosclerotic Peripheral Vascular Disease Interdisciplinary Working Group; Cardiovascular Nursing Council; Clinical Cardiology Council; Nutrition, Physical Activity, and Metabolism Council; and the Quality of Care and Outcomes Research Interdisciplinary Working Group: *Circulation*, 2006; 113: 85-151
    - Drug Insight: Statin and Stroke (Nature *Clin Practice Cardiovascular Med*. 2005; 2: 576-584)
    - Treat to New Targets (TNT). *N Engl J Med*. 2005;352:1425-1435)
    - Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL). *N Engl J Med*. 2006; 355:549-559)

Dr. Axelrod said that the Committee previously discussed that the question is not as much which drug but if to treat. In diabetic patients, the need to treat has escalated. For the rest of the population, the number of people it takes to treat to prevent an event and the cost of the drug reverses the return on investment (ROI). The question is how to spend money wisely to have the most positive impact on the largest number of people. How do we make better medicine both financially and clinically oriented? Generic simvastatin is an example where you can save billions of dollars while maintaining the same treatment and improving the treatment with the dollars saved.

Dr. Nixon responded that in high and very high-risk patients the best outcomes are seen with the use of the most potent drugs. He has an obligation to treat his patients with the most optimal medication.

Dr. Nixon and Dr. Axelrod discussed the difference between primary and secondary treatment and some new initiatives attempted in England.

Tim Jennings asked how you treat primary prevention of stroke.
Dr. Nixon responded that he adheres to the published guidelines that follow an LDL target and uses a statin to lower the LDL and achieve that target level.

Ms. Abernathy asked, when you titrate you start at the lowest dose and titrate up? Or do you do not start at the highest dose and titrate down?
Dr. Nixon responded, yes, clinicians are trained with all medications to start at the lowest doses and titrate to higher ones.

Mark Henderson, Ph.D., Senior Clinical Account Manager, at AstraZeneca discussed HMG CoA Reductase Inhibitors (Statins) ~ Crestor

The optimal LDL for everyone is less than 100 mg/dl. He reviewed two new demographic trials.
The ARIES trial evaluated the efficacy of rosuvastatin (10mg and 20mg) compared to atorvastatin (10mg and 20mg) in the African-American population over a 6-week period. LDL-C was reduced to a significantly greater extent with rosuvastatin 10mg compared to atorvastatin 10mg. Rosuvastatin is a statin capable of providing significant improvements in the lipid profile in a wide variety of adult patient populations with hypercholesterolemia, with and without hypertriglyceridemia, regardless of race, gender, or age. In a dose-ranging study, rosuvastatin produced dose related reductions in LDL-C of 45-63% across the dose range of 5-40mg once daily, decreased TG between 10-35%, and increased HDL-C between 8% and 14%. Rosuvastatin is generally well tolerated and adverse reactions have usually been mild and transient. The post-marketing safety profile of rosuvastatin is consistent with that seen in the clinical trial program and similar to that of other currently marketed statins.

Margaret Savage, MD, MPH, Medical Science Specialist at Merck/Schering-Plough Pharmaceuticals discussed HMG CoA Reductase Inhibitors (Statins) ~ Vytorin

Vytorin® contains simvastatin and ezetimibe. It is indicated as adjunctive therapy to diet, when diet alone is not enough, for the reduction of elevated total cholesterol, LDL cholesterol, and to increase HDL cholesterol in patients with primary hypercholesterolemia or mixed hyperlipidemia. Vytorin® works at reducing cholesterol levels by dual inhibition, inhibiting the production of cholesterol in the liver and blocking the absorption of cholesterol in the intestine, including cholesterol from food. According to the speaker, this is the only drug that does this.

Two studies in 2006 one against Lipitor® and one against Crestor® both showed that Vytorin® is more effective at lowering LDL and increasing HDL at all doses compared to the other two products, ranging from the usual recommended starting doses to the maximum approved doses. Both studies are now included in the label for Vytorin®. Vytorin® is proven to have an excellent safety profile.

John D. Ostrosky, PharmD, Senior Clinical Education Manager at Pfizer Inc at HMG CoA Reductase Inhibitors (Statins) ~ Lipitor

Dr. Ostrosky reviewed a handout given to the Committee. He noted that a statin such as Lipitor® could be effectively used to treat high LDL cholesterol and high triglycerides – rather than using two lipid lowering agents (e.g., a statin and a fibrate) that individually manage both problems. In the "CAPISH" study, Krasuski and colleagues (Mayo Clin Proc 2005;80:1163-8) confirmed that patients who failed or were intolerant to simvastatin and who were receiving a fibrate could be switched to atorvastatin monotherapy. The result is a statistically significantly lower average LDL cholesterol level and a comparable triglyceride level – with a significantly lower frequency of CPK elevations.

Dr. Ostrosky discussed trends as observed by Pfizer following the implementation of the PDL in 2003.

He reviewed a comprehensive analysis of clinical atorvastatin trials (Newman et al.; Am J Cardiol 2006;97:61-7.) This analysis found no dose-related differences in musculo-skeletal adverse events between 10 and 80 mg daily doses of atorvastatin. This statement cannot be made for the other PDL statins.

In Dr. Ostrosky's opinion, the addition of Lipitor® (without a step-edit) to the Virginia Medicaid PDL would allow physicians to prescribe just one agent that could effectively lower both LDL and triglyceride levels, minimizing pill burden, safety concerns and drug-drug interactions (that are associated with the use of statins and fibrates), as well as improve outcomes.

Gill Abernathy reviewed HMG CoA Reductase Inhibitors (Statins)

Many studies and meta-analysis have been conducted over the past few years concerning products for lipid lowering. The most recent trials have confirmed the benefit of reducing LDL-c below 100 mg/dl. For a number of high-risk people (such as people with CHF, Diabetics, two CHD risk events, or people prone to developing an ischemic event), the new goal is less than 70 mg/dl.
All of the HMG CoA Reductase Inhibitors can safely reduce LDL-C by the 30% required in most patients to reach goal. In patients who require a more significant reduction in LDL-C, the use of combination therapy with a lipotropic agent of a different class is often indicated. Combination therapy may avoid the increase in adverse effects often seen with higher doses of HMG CoA Reductase Inhibitors.

The FDA approved a new indication and dosage regimen for Lescol® (Fluvastatin) and Lescol XL® on April 10, 2006. They are both now approved for the treatment of heterozygous familial hypercholesterolemia in adolescent boys and postmenarchal girls, ages 10 to 16 years, with a recommended dosing range of Lescol® capsules 20 to 40 mg twice daily or Lescol XL® 80mg tablet once daily. Additionally, Lescol XL® 80mg is now approved to be administered at any time of day instead of in the evening.
New generic statins:

- FDA approved first-time generic pravastatin (Pravachol®) on April 24, 2006. Pravastatin sodium tablets are available in 10mg, 20mg and 40mg tablets.
- FDA approves first-time generic simvastatin (Zocor®) on June 23, 2006 to treat hypercholesterolemia (high cholesterol). Simvastatin tablets are available in 5mg, 10mg, 20 mg, 40mg, and 80mg tablets.

Gill Abernathy brought to the attention of the Committee that if a patient does not reach goal it is not difficult to receive one of the other products. She read the HMG CoA Reductase Inhibitors criteria for obtaining prior authorization.

Gill Abernathy motioned that the HMG CoA Reductase Inhibitors (Statins) remain PDL eligible.
The motion was seconded.
The Committee voted unanimously to consider the HMG CoA Reductase Inhibitors (Statins) as PDL eligible.

Gill Abernathy reviewed Lipotropics Non-Statins: Fibric Acid

Fibric acids have been shown to reduce the risk of CHD in patients with high triglycerides and low HDL. The FDA has approved a new indication for Zetia®; an active inhibitor of the absorption of dietary and biliary cholesterol and related phytosterols by inhibition of the transport of cholesterol across the intestinal wall. It is now approved to be administered in combination with fenofibrate, as adjunctive therapy to diet, for the reduction of elevated total cholesterol, LDL-C, Apo B and non-HDL-C in patients with mixed hyperlipidemia.

Gill Abernathy motioned that the Lipotropics Non-Statins Fibric Acid class remain PDL eligible**.**
The motion was seconded**.**
The Committee voted unanimously to consider the Lipotropics Non-Statins Fibric Acid as PDL eligible.

Jene' Martins Richards, PharmD, Medical Science Liaison at Kos Pharmaceuticals, Inc. discussed Lipotropics Non-Statins: Niacin Derivatives ~ Niaspan

Niaspan® is the only once daily prescription extended release niacin.
Niaspan® is currently on the Virginia Medicaid PDL and Kos Pharmaceuticals hopes to retain the status.
The advantages to Niaspan® are one pill, one co-pay, increased compliance, and greater reduction in cardiovascular risk by increasing HDL-C and lowering LDL-C.
The results of a recent ARBITER 3 study were discussed.

- Objective of ARBITER 3 was a continuation of the ARBITER 2 trial, which showed that extended-release niacin (ERN) when added to statin monotherapy slowed the progression of carotid atherosclerosis over 12 months. Whether longer treatment with ERN would have a greater effect on carotid intima media thickness (CIMT) is unknown.
- Main outcome measures were within the group change in CIMT and HDL-C in patients receiving placebo for 12 months, ERN 12 months (12 months of Arbiter 2 and 12 months placebo cross-over Arbiter 3), and total 24 months in continuation group.
- Results of the trial are in the ERN 12-month group (125 patients) there was net regression of -0.027. In the 24- month continuation group there was regression of -0.040. Controlling for changes in TG or LDL-C, only changes in HDL-C were independently associated with regression of CIMT.
- The study concluded that by adding just one gram of Niaspan® to patients on stable statin therapy with LDL-C's less than 100mg/dl, resulted in stabilization of the plaque in Arbiter 2, and continuing for another 24 months, resulted in significant regression.

Gill Abernathy reviewed Lipotropics Non-Statins: Niacin Derivatives

Niacin is believed to inhibit hepatic production of triglycerides resulting in a reduction of VLDL that is available for conversion to LDL-C.
There is a new strength of Advicor® (lovastatin/niacin) approved by the FDA for an extended-release oral tablet to contain niacin 1000mg/lovastatin 40mg.

Gill Abernathy motioned that the Lipotropics Non-Statins Niacin Derivatives remain PDL eligible.
The motion was seconded.
The Committee voted unanimously to consider the Lipotropics Non-Statins Niacin Derivatives as PDL eligible.

Andy Katsiaras of Daiichi Sankyo, Inc discussed Angiotensin Receptor Blockers (ARBs) ~ Benicar®

Benicar® is a once daily treatment for the treatment of hypertension; it is a first line therapy either alone or in combination with other agents. It is available in 5, 20 and 40 mg doses. In a review of seven clinical trials verses placebo using either 20 or 40 mg doses, blood pressure reduction was achieved.
The most common adverse drug reaction is dizziness. It is also available as a combination drug with hydrochlorothiazide. He asked that the Committee consider adding Benicar® and Benicar HCT® to the PDL as preferred.

Gill Abernathy reviewed Angiotensin Receptor Blockers

Some head-to-head, antihypertensive comparative trials have been conducted between ARBs but they were for short durations. Long-term clinical outcomes trials have not directly compared the agents in this class. Cardiovascular outcomes data is available from large clinical trials comparing ARBs to other types of antihypertensive agents.

All of the ARBs lower blood pressure to a similar degree. Limited data suggest that Diovan® and Avapro® at higher doses offer a greater decrease in blood pressure (BP) than Cozaar®. Atacand® has been shown to lower BP to a greater degree than Hyzaar®. All ARBs are generally well tolerated.
In addition to lowering BP, the ARBs are proven to delay the progression of diabetic nephropathy; this is believed to be a class effect but requires more data.

As with ACE Inhibitors, the ARBs are classified as Pregnancy Category C for the first trimester of pregnancy and as Pregnancy Category D for the second and third trimesters.
Diovan HCT® (valsartan/hydrochlorothiazide) has two new strengths approved by the FDA they are tablets of 320mg/12.5mg and 320mg/25mg.
The current criterion was read.

Gill Abernathy motioned that the Angiotensin Receptor Blockers be PDL eligible.
The motion was seconded.
The committee voted unanimously to consider the Angiotensin Receptor Blockers as PDL eligible.

Edgar Gonzales, Pharm D, President and CEO of Capital Pharmacy Consultants, representing for King Pharmaceuticals discussed ACE Inhibitors -Altace®

Dr. Gonzales was a member of the HOPE trial and realizes that there are many ACE inhibitors (ACEIs) available but believes that Altace® is the one ACEI that consistently shows its superiority. He is asking the Committee to allow Altace® to be a preferred product in Virginia. His experience leads him to question the class effect with ACE Inhibitors. He cited the HOPE and HOPE-TOO trial investigators' findings on the long-term effects of ramipril on cardiovascular events and on diabetes as his reason to question class effect. He stated that the results of the HOPE study extension (*Circulation*, 2005; 112: 1339-1346) shows evidence that Altace® has a superior effect on secondary endpoints including a reduced chance of a combined cardio-renal outcome. Specifically, cardiovascular secondary endpoints included clinical or silent myocardial infarction, stroke, cardiovascular death, revascularization procedures, heart failure, and new-onset angina with objective evidence of ischemia. He encourages treating specific outcomes (stroke, kidney failure, etc) not blood pressure.

Gill Abernathy reviewed Angiotensin Converting Enzyme Inhibitors (ACE Inhibitors)

ACE inhibitors are well-established and considered first line therapy for essential hypertension. There are compelling indications for the use of ACE inhibitors with other disease states such as CHF, post-MI, high-risk cardiovascular disease, diabetes, chronic kidney disease and recurrent stroke prevention. With the numerous clinical trials during the 80's, 90's and 21st century, there is little evidence that one ACE is better than another for the approved indications. Experience from comparative trials suggests that there are few differences between ACE inhibitors in terms of antihypertensive efficacy when equipotent doses of each agent are used. One issue recently raised in the June 2006 FDA Alert relates to ACE Inhibitors and Pregnancy. An article published on June 8, 2006, in the *New England Journal of Medicine* reports that infants of mothers who had received angiotensin-converting enzyme inhibitors (ACE inhibitors) during the first trimester of pregnancy had a greater risk of major congenital malformations, as compared to infants who had not been exposed to these medications during the first trimester of pregnancy. Current labeling indicates that ACE inhibitors are classified as Pregnancy Category C for the first trimester of pregnancy and as Pregnancy Category D for the second and third trimesters of pregnancy. Prescribing information also recommends that ACE inhibitors be discontinued as soon as possible if a patient becomes pregnant. This newly published data is preliminary; therefore, at this time, the FDA does not plan to change current pregnancy categories for these medications. Methyldopa, beta-blockers and vasodilators are preferred medications for treatment of chronic hypertension during pregnancy to provide safety of the fetus.

Lotrel (Amlodipine/ Benazepril), an ACE inhibitor/calcium channel blocker combination product for treatment of hypertension is now available in two new dosage strengths: 5mg/40mg and 10mg/40mg. FDA approved new dosage strengths on April 11, 2006.

Tim Jennings motioned that the Angiotensin Converting Enzyme Inhibitors be PDL eligible.

The motion was seconded.
The Committee voted unanimously to consider ACE Inhibitors as PDL eligible.

Kerry Cunningham of GlaxoSmithKline discussed Beta Blockers ~ Coreg
Coreg is the only Beta Blocker with an FDA indication for post MI and CHF. The following points were made:

- Based on recent clinical studies, the American Association of Clinical Endocrinologists (AACE) made several specific recommendations in their recent update to the "Medical Guidelines for Clinical Practice for the Diagnosis and Treatment of Hypertension". These guidelines were published in Endocrine Practice Vol 12, No. 2 March/April 2006.
- The AACE Hypertension Task Force specifically points out the potential benefit by utilizing beta-blockers that block both alpha and beta receptors in treating the patient with hypertension and Type 2 diabetes mellitus.
- The AACE Guidelines also refer to studies with carvedilol that have been shown to increase insulin sensitivity, while atenolol, metoprolol and propranolol all have been shown to decrease insulin sensitivity.

Gill Abernathy reviewed Beta Blockers
Beta blockers have been available and used in the United States for many years. They have been used for various indications such as for hypertension, treatment of angina and /or arrhythmias and heart failure. Now their role is changing. In the current JNC-VII guidelines, they are no longer considered first line therapy for hypertension. First line is diuretics. Current JNC-VII guidelines suggest beta-blockers be used for those patients with compelling indications such as ischemic heart disease or angina. We now see increasing use of long-acting beta blockers in the treatment of heart failure. All three long-acting beta blockers have clinical data to support their use in heart failure management. Recent guidelines from the American College of Cardiology and the American Heart Association do not recommend one beta blocker but three to treat heart failure. Two of these three medications have FDA indications; Toprol XL® and Coreg®. Ms. Abernathy asked the Committee to consider including one of the long-acting beta blockers as preferred for CHF.

Gill Abernathy motioned that the Beta Blockers be PDL eligible and to include one of the long-acting beta blockers as preferred for CHF.
The motion was seconded.
The Committee voted unanimously to consider the Beta Blockers as PDL eligible.

Gill Abernathy reviewed Calcium Channel Blockers (CCBs)
The benefits of calcium channel blockers in controlling angina and hypertension are clearly documented. According to the JNC-VII guidelines, there are compelling indications for the use of CCBs in high-risk CHD patients and diabetics.

Gill Abernathy motioned that the Calcium Channel Blockers be PDL eligible.
The motion was seconded.
The Committee voted unanimously to consider the Calcium Channel Blockers as PDL eligible.

Gill Abernathy reviewed Phosphodiesterase 5 Inhibitor for Pulmonary Arterial Hypertension
No change in this class since Revatio® entered the market last year.

Mark Oley motioned that the Phosphodiesterase 5 Inhibitor be PDL eligible.
The motion was seconded.
The Committee voted unanimously to consider the Phosphodiesterase 5 Inhibitor as PDL eligible.

William C. Rees, MD, MBA, FAAP, of the private practice of Drs. Balsamo, Arnoldson, Rees and Garner discussed Beta Adrenergics ~ Levalbuterol (Xopenex®)

Dr. Rees' discussion points were as follows:

1. Clinical efficacy and safety of Levalbuterol (Xopenex®) Nebulized Solution and Metered Dose Inhaler has been substantiated in the past several years. Continued clinical research has also substantiated its value.
2. Dr. Rees has maintained an active clinical practice with a large patient population, both commercial insurance and Medicaid, with asthma and has been a coauthor of clinical published clinical research articles, as listed on his CV.
3. Maintaining access to a very efficacious and safe rescue medication is critical to primary care medicine. Xopenex® is the only alternative bronchodilator to racemic albuterol.
4. In addition to maintaining access to the nebulized solution of levalbuterol, the meter dose inhaler is the only single isomer HFA available. There are presently only two HFA products on the market and one of the two is a racemic albuterol. There have recently been random shortages of CFC products and eventual discontinuation of CFC products is expected in the year 2008. Continuity of care, and access to appropriate medication, is critical in this patient population.

Additional information has been published since October 2005 that is pertinent for the Committee to consider for the PDL Phase 1 Annual Review of Beta Adrenergics, specifically levalbuterol nebulized solution and metered dose inhaler (HFA): Schreck, et al. Comparison of racemic albuterol and Levalbuterol in the treatment of acute asthma in the ED. *American Journal of Emergency Medicine* (November 2005) 23, 842-847.

Gill Abernathy reviewed Beta Adrenergics

The switch of propellants to non-ozone depleting agents such as hydrofluoroalkane (HFA) is well underway. Most products are now available in a HFA formulation. Equivalence has been shown for both the treatment and prophylactic indications for albuterol, between the chlorofluorocarbons (CFC) and the HFA formulations.

Gill Abernathy motioned that the Beta Adrenergics be PDL eligible.
The motion was seconded.
The Committee voted unanimously to consider the Beta Adrenergics as PDL eligible.

Dr. Kevin Cooper, a pulmonary disease and critical care physician at MCV VCU discussed COPD-Anticholinergics ~ Spiriva®

Dr. Cooper has no financial ties to the manufacturer of Spiriva®.
There are twenty-four million people in the US with COPD and the majority 70 % are under 65 years of age. The GOLD guideline calls for the use of both short and long acting agents. The short acting is indicated for mild disease and the long acting for mild to moderate. His clinical experience has shown that tiotropium is better than ipratropium. Dr. Cooper noted that with COPD the goal is to improve lung function and as with hypertension, people with COPD are on more medications. As the disease becomes worse, more medications are needed. COPD places a substantial financial burden on state Medicaid programs. He referenced the findings from the study Marton. J, Boulanger L, et al. (Assessing the costs of chronic obstructive pulmonary disease: The state medicaid perspective. *Resp Medicine*. October 2005).

Gill Abernathy reviewed COPD- Anticholinergics

The FDA approved a long-acting inhalation solution on October 10, 2006 made by Sepracor Inc. It is estimated that by the second quarter of 2007, the Brovana (arformoterol tartrate) inhalation solution for the long-term, twice-daily treatment of bronchoconstriction in patients with chronic obstructive pulmonary disease will be available**.** This is the first long-acting beta-2-receptor agonist formulated as an inhalation solution for use with a nebulizer (*R*-enantiomer of formoterol). The labeling recommends a dosage of 15 mcg in the morning and evening. As with the product labeling for other long-acting beta-2-receptor agonists, the

labeling for arformoterol includes a prominent warning about the possible increased risk of asthma-related death in patients who use the drug. In addition, there is an FDA-approved medication guide that pharmacists must give patients when dispensing Brovana®.

Mark Oley motioned that the COPD- Anticholinergics be PDL eligible.
The motion was seconded.
The Committee voted unanimously to consider the COPD- Anticholinergics as PDL eligible.

Dr. Gokul Gopalan, MD, MPH, Regional Medical Science Specialist, Global Medical Affairs for Schering-Plough Pharmaceuticals discussed Inhaled Corticosteroid ~ Asmanex®
Asmanex® is first line therapy in the treatment of mild to moderate asthma. It is used once a day for maintenance therapy. It is for ages 12 years and older. It is not indicated for acute bronchospasm. In published articles, Asmanex® is indicated to decrease nighttime waking and reduces albuterol PRN usage. In patients with severe persistent asthma, the use of Asmanex® reduces the need for oral and inhaled corticosteroids. It is very safe with only 1 percent oral bioavailability. It has mild to moderate side effects.

Gill Abernathy reviewed Inhaled Corticosteroids
The newest agent, Asmanex®, represents an additional option in the class' arsenal. There are no comparative efficacy trials available to date that compare Asmanex® to other inhaled corticosteroids.

On November 18, 2005, FDA alerted health care professionals and patients that several long-acting bronchodilator medicines have been associated with possible increased risk of worsening wheezing (bronchospasm) in some people, and requested that manufacturers update warnings in their existing product labeling. This information has now been included in the updated labeling. Currently, the FDA has approved new safety labeling and medication guides for patients for Serevent Diskus®, Advair Diskus®, Foradil®, and Advair HFA®.

Mark Oley motioned that Inhaled Corticosteroids be PDL eligible.
The motion was seconded.
The Committee voted unanimously to consider Inhaled Corticosteroids as PDL eligible.

Dr. Gokul Gopalan, MD, MPH, Regional Medical Science Specialist, Global Medical Affairs for Schering-Plough Pharmaceuticals discussed Nasal Steroid ~ Nasonex®
Nasonex® is one of the most commonly prescribed products for allergic rhinitis. It can be used to treat symptoms or prophalactically to prevent symptoms. There is no history of suppression. It can be used in children as low as 2 years of age. Dr. Gopalan states that one place where Nasonex® stands out compared to other similar products in its class is in preference. Patients prefer to use Nasonex® compared to other products.

Gill Abernathy reviewed Nasal Steroids
There have been no changes to this class since new generic last year of Flunisolide (Nasarel).

Mark Oley motioned that Nasal Steroids be PDL eligible.
The motion was seconded.
The committee voted unanimously to consider Nasal Steroids as PDL eligible.

David Glazier, MD, Director, Virginia Urology Continence Center and Practicing Urologist discussed Urinary Tract Antispasmodics ~ Detrol LA®
Dr. Glazier is the Director of the Clinical Trial Department and has done clinical trials with many of the drug companies. Detrol LA® is effective in overactive bladder. It is effective in 80% reduction of incontinence and 40% reduction of nighttime frequency.

It is safe across all age spectrums. It does not interact with the metabolism of other drugs and there is no CYP action. It is not lipophilic and does not cross the blood brain barrier, therefore, there are few CNS side effects. It is overall a safe and effective agent.

Mark Oley reviewed Urinary Tract Antispasmodics
There have been no changes in this class since the last review.

Mark Oley motioned that Urinary Tract Antispasmodics be PDL eligible.
The motion was seconded.
The Committee voted unanimously to consider Urinary Tract Antispasmodics as PDL eligible.

David R. Spiegel, MD, Assistant Professor, Department of Psychiatry and Behavioral Sciences at Eastern Virginia Medical School discussed Other Sedative Hypnotics ~ Rozerem® (Ramelteon)
Dr Spiegel is on the speaker board for Takeda.
Dr. Spiegel provided the following clinical and scientific data about the utilization of ramelteon for acute and chronic insomnia:

- Ramelteon is the only non-scheduled prescription insomnia agent available in the United States, and as such, has no abuse or addiction potential.
- Ramelteon has a unique mechanism of action it is the only selective melatonin receptor agonist available in the United States and does not act by CNS depression via histamine-1 receptor blockade, nor agonism at the GABA-A or opiate receptors. As such, this decreases the risk of next day cognitive and psychomotor effects. Just as important, this could decrease the risk of falls and hip fractures in the elderly.
- Additionally, in the elderly with neurodegenerative disease (i.e., dementia), circadian dysrhythmias may be at the cause of insomnia in this patient population. Ramelteon's unique mechanism of action specifically addresses this issue.
- Indicated by the FDA to treat both transient and chronic insomnia
- Approved for short term and long-term use
- Controlled studies prove efficacy in the adult and geriatric populations.
- Clean safety profile.
- Lacks the GABA-A alpha subunit side effects, i.e., sedation and amnesia.
- Lacks interaction with multiple receptors limiting the potential for serious adverse effects, as can occur with sedating antidepressants

Maha Alattar, MD, Assistant Professor of Neurology at University of North Carolina discussed Other Sedative Hypnotics ~ Lunesta
Dr. Alattar advocates the use of non-benzodiazepine hypnotics for treatment of insomnia. She discussed the negative impact on daytime function because of insomnia. She cited the study by Roth T, Walsh J, Krystal A, Wessel T, Roehrs T. -- An evaluation of the efficacy and safety of eszopiclone over 12 months in patients with chronic primary insomnia. *Sleep Medicine* 2005;6:487-495. She notes this study showed efficacy for both sleep induction and sleep maintenance without tolerance after long-term use. There was a significant improvement in sleep and daytime function at 6 months, which was sustained for an additional 6 month during the open label trial.

Also cited was the study by Fava M, McCall W, Krystal A, Wessel T, Rubens R, Caron J, Amato D, Roth T. -- Eszopiclone Co-Administered with Fluoxetine in Patients with Insomnia Coexisting with Major Depressive Disorder. *Biol Psychiatry* 2006; 59:1052-1060. This study showed efficacy for both sleep induction and sleep maintenance without interfering with SSRI treatment. The eszopiclone/fluoxetine co-therapy was well tolerated and associated with rapid and substantial improvement (sleep and antidepressant effect). She closed noting the improvement in sleep architecture with Lunesta® compared with a benzodiazepine.

Dr. Nichols asked in terms of nightly benefit, how much benefit did people receive from using Lunesta®?
Dr. Alattar responded that the benefit was not seen in total sleep time, the benefit is in their wakening time.

Jeff M. Sommers, M.D., Psychiatrist, Insight Physicians, P.C. discussed Other Sedative Hypnotics ~ Ambien CR®

Dr. Sommers noted that he has no financial ties. Sleep and the importance of insomnia have a large impact on his patient population. Approximately 10% of all Americans have chronic insomnia and another 30% have transient insomnia. People with depression will respond more quickly to medication if they can resolve the insomnia issue. Insomnia has a large impact on mental and cognitive status of an individual. With Ambien CR®, they have developed a product that helps the individual go to sleep with the immediate release and stay asleep with the controlled release product. This creates better function throughout the next day. There are no residual effects the next day. There is minimal risk of tolerance.

Dr. Nichols asked about the benefit compared to placebo.
Dr. Sommers replied that he believes that it is 30 minutes more per night then you start to add up 10 to 12 hours per month.

Dr. Nichols asked if there are any studies with Ambien CR® and sleep hygiene?
Dr. Sommers replied that sleep hygiene could be effective in transient insomnia; sleep hygiene is not effective in chronic insomnia.

Tim Jennings asked if there is an advantage in cycling therapy?
Dr. Sommers answered that someone with transient insomnia does not take it nightly. They do cycle.

Gill Abernathy asked if there was any group that he would not feel comfortable prescribing Ambien CR®?
Dr. Sommers answered that he may not be comfortable prescribing Ambien CR to people who abuse alcohol and those with sleep apnea.

Teresa McRorie Osborn, Pharm.D. BCPS, Regional Scientific Manager, Neuroscience at Takeda Pharmaceuticals discussed Other Sedative Hypnotics ~ Rozerem®

Rozerem® is safe and effective in both adult and elderly patients. It is effective in both chronic and transient insomnia. It is safe for long-term use and has shown no evidence of rebound insomnia. There is no abuse liability with Rozerem® or dependency. It may be useful in people with a history of dependence. Rozerem® is safe in patients with obstructive sleep apnea as well as chronic obstructive pulmonary disease. In recent studies, an improvement in sleep latency and total sleep time was sustained over a year period.

Mark Oley reviewed Benzodiazepine Sedative Hypnotics

There has been no change in this class since the last review. There is a quite a bit of variability in onset and duration of action that may make one preferable to another. This allows the physician to identify the product that matches the patient's insomnia. They are all available as generics.

Mark Oley motioned that Benzodiazepine Sedative Hypnotics be PDL eligible.
The motion was seconded.
The committee voted unanimously to consider Benzodiazepine Sedative Hypnotics as PDL eligible.

Mark Oley reviewed Other Sedative Hypnotics

Last year the Committee discussed at length the newest product in this class, ramelteon. Ramelteon has been available for a year now. Unlike other drugs in this class, it is not a sedative and is not a controlled substance. It is not associated with tolerance, dependency, or rebound. It is, however, effective only in reducing time to sleep onset.

Sonata®'s indications changed to remove the limit of 7 to 10 days use and the limit of a one-month supply. Dr. Axelrod asked if the current PDL criteria have quantity supply limits or duration of therapy for either of the Sedative Hypnotics classes.
Gill Abernathy read the current criteria to the Committee.
The Committee discussed the current criteria, clinical standards for sedative hypnotics today, and proposed changes. The outcomes of the clinical discussions were the following recommendations.

Dr. Axelrod outlined the motion as follows:

1) Table the discussion regarding duration of therapy and quantity supply of sedative hypnotics until the Spring 2007 meeting when they can review the literature and some statistics
2) Make the Other Sedative Hypnotics class PDL eligible
3) Change the current criteria to read "for patients age 65 and older, Rozerem®, Ambien® or Lunesta® may be approved after a trial of trazodone (duration = at least one month). It is not necessary for patients ≥ 65 to try a benzodiazepine if they have had a trial of trazodone."

Tim Jennings presented the motion as reviewed by Dr. Axelrod.
The motion was seconded.
The committee voted unanimously to:

1) Review the literature and some statistics at the spring meeting concerning the duration and quantity supply of sedative hypnotics
2) Make the Other Sedative Hypnotics PDL eligible
3) Change the current criteria to read "For patients age 65 and older, Rozerem®, Ambien® or Lunesta® may be approved after a trial of trazodone (duration = at least one month). It is not necessary for patients ≥ 65 to try a benzodiazepine if they have had a trial of trazodone."

John C. Frey R.Ph., Regional Account Manager for Santarus, Inc. discussed Proton Pump Inhibitors (PPIs) ~Zegerid®

There are two types of PPIs immediate release – Zegerid and delayed release – all other PPIs.
All delayed release are similar to one another. Acid degrades the active ingredient of PPI's. They must protect the drug from the acid medium of the stomach. All commercial products are enteric coated to protect from acid (including suspensions and dissolving tablets), this means that all have delayed absorption and bioavailability. Studies suggest modest benefit of one delayed release agent over another. All delayed release PPIs are dependent on food stimulus for optimum pump blockade since only active proton pumps can be inhibited. The ACG guidelines state "Oral delayed release PPIs are optimally dosed prior to a meal". Immediate release Zegerid® is a combination of the active ingredients, omeprazole and the antacid sodium bicarbonate. It is marketed as a 40mg and 20mg, powder for oral suspension and oral capsule. Both formulations have similar pharmacokinetics and pharmacodynamics. Sodium bicarbonate buffer neutralizes gastric acidity and prevents omeprazole degradation. With no enteric coating to hinder absorption, it is absorbed immediately in the small intestine giving peak plasma levels in 30 minutes. Unlike the delayed release PPI, data has shown Zegerid® is effective when dosed on an empty stomach eliminating the need for food coordination. Zegerid® is the first and only PPI FDA approved for the reduction of risk of upper GI bleeding in critically ill patients. Zegerid®, when dosed at bedtime, is more effective in reducing nighttime gastric acidity than pantoprazole. Recent head-to-head comparison study presented recently at DDW has shown that Zegerid® is more effective in reducing nighttime intragastric acidity than esomeprazole and lansoprazole when dosed at bedtime. Zegerid® has been shown to maintain gastric pH>four for 18.6 hours. As a powder for oral suspension, Zegerid® may be titrated for specialty populations.

Mark Henderson, Ph.D., Senior Clinical Account Manager at AstraZeneca discussed Proton Pump Inhibitors ~ Nexium®

Nexium® has a new indication of use in adolescents (age 12 – 17 years). Nexium 20 mg or 40 mg once daily is approved for the short-term treatment of GERD for up to 8 weeks in adolescent patients aged 12 to

17 years. Nexium pharmacokinetics in adolescent patients were similar to those observed in adult patients with symptomatic GERD. In addition, no new safety concerns were identified in a study that evaluated the safety and tolerability of esomeprazole 20mg and 40 mg for up to 8 weeks in 149 adolescent patients with clinically diagnosed GERD. In addition, Nexium has greater efficacy in healing of erosive esophagitis (EE) than omeprazole, lansoprazole, and pantoprazole through 8 weeks. EE is estimated to be present in approximately 30% of all GERD. Before the approval of esomeprazole, no other PPI was shown to have greater EE healing efficacy than the prototype PPI, omeprazole 20 mg. Nexium is the first PPI to demonstrate a statistically significant difference in the healing of EE when compared to another PPI. Several large, multicenter, randomized, double blind, placebo controlled, head-to-head studies have examined the EE healing rates of esomeprazole versus omeprazole, lansoprazole, and pantoprazole. In a multicenter, randomized, double-blind trial, Katz et al evaluated the relationship between the percentage of time with pH > 4 and the healing of EE and the symptomatic control of GERD with esomeprazole 10 mg or 40 mg once daily for 4 weeks in patients with LA grade C or D. Complete healing of EE was demonstrated to be positively associated with greater percentage of time intragastric pH was > 4.

Mark Oley reviewed Proton Pump Inhibitors (PPIs)
Numerous comparative published studies of the various PPIs have failed to show a significant benefit of any one agent over another.
Zegerid® (Omeprazole/ sodium bicarbonate/ magnesium hydroxide) is now available in a chewable tablet, formulated with both sodium bicarbonate and magnesium hydroxide for short-term treatment of active duodenal ulcer, heartburn and other symptoms associated with GERD, short-term treatment and maintenance healing of erosive esophagitis, and short term treatment of active, benign gastric ulcer.

Dr. Axelrod confirmed that the OTC issues and generic supply is no longer an issue with this class.

Gill Abernathy motioned that Proton Pump Inhibitors be PDL eligible.
The motion was seconded.
The Committee voted unanimously to consider Proton Pump Inhibitors as PDL eligible.

Mark Oley reviewed H2 Antagonists
There have been no changes in this class since the previous review. There is little difference between the effectiveness of the available products in their indicated uses.

Mark Oley motioned that H2 Antagonists be PDL eligible.
The motion was seconded.
The committee voted unanimously to consider H2 Antagonists as PDL eligible.

Mark Oley reviewed Second Generation Antihistamines (LSAs)
There have been no changes in this class since the previous review. There is little difference among the products currently available. All agents in this category appear to be similar in efficacy.

Tim Jennings motioned that Second Generation Antihistamines be PDL eligible.
The motion was seconded.
The Committee voted unanimously to consider Second Generation Antihistamines as PDL eligible.

Mark Oley reviewed Electrolyte Depleters
There have been no changes in this class since the previous review.

Tim Jennings motioned that Electrolyte Depleters be PDL eligible.
The motion was seconded.
The committee voted unanimously to consider Cox-2 Inhibitors as PDL eligible.

Mark Oley reviewed Cox-2 Inhibitors
No change with Celebrex® over the past year. This class, Cox-2 Inhibitors, will be added to the Nonsteroidal anti-inflammatory drugs for review from this meeting forward.

FDA approved a first-time generic meloxicam (Mobic) to treat osteoarthritis.

Tim Jennings motioned that Cox-2 Inhibitors be PDL eligible.
The motion was seconded.
The committee voted unanimously to consider Cox-2 Inhibitors as PDL eligible.

Mark Oley reviewed Topical Immunomodulators
The FDA approved updated labeling for Elidel® Cream (pimecrolimus) and Protopic® Ointment (tacrolimus) which are topical agents for the treatment of mild to moderate atopic dermatitis (eczema). Although a causal link has not been established, rare reports of cancer, such as skin cancer and lymphoma, have been reported in patients using these products. On January 19, 2006, the FDA announced its approval of updated labeling for these products. This is to include a boxed warning about a possible risk of cancer and a Medication Guide to be distributed to help make certain that patients are aware of this concern. New labeling includes clarification that these agents are recommended only as second-line treatment options and that treatment with these products of children less than two years of age is not recommended. Although studies are underway to try to answer questions about cancer risk, they may not be concluded for years and these drugs do offer treatment benefit when used appropriately. They are intended for short term use and if longer treatment is required, can be repeated after a period of time off treatment. Patients are advised to contact their physician if symptoms become worse, if an infection develops, or if symptoms do not improve within six weeks of therapy. Last year this Committee anticipated these warnings and the current criteria meet these guidelines.

Tim Jennings motioned that Topical Immunomodulators be PDL eligible**.**
The motion was seconded.
The Committee voted unanimously to consider Topical Immunomodulators as PDL eligible.

Tim Jennings requested information on the package size being used for these products.
This information will be obtained and sent to the Committee.

COMMENTS FROM OFFICE OF THE ATTORNEY GENERAL
Ms. Reatha Kay from the Attorney General's office stated that under the Virginia Freedom of Information Act (FOIA), specifically Virginia Code section 2.2-3711, a public body such as the P&T Committee, may go into a closed session for any of the 33 reasons listed in that statute. The discussion of manufacturer and wholesaler prices is not one of the 33 reasons listed.

She stated the Attorney General strongly supports the principles of open government embodied by the FOIA and believes in the opportunity of the Commonwealth's citizens to witness the operation of government to the fullest extent.

Federal Law 42 U.S.C. 1396r-8(b)(3)(D) requires such pricing information to be kept confidential. On this point, federal law supersedes the Virginia FOIA. Since the P&T Committee must discuss this pricing information as part of its duties, pursuant to federal law a confidential meeting must occur for the consideration of this pricing information she cautioned only this confidential information should be discussed.

Mark Oley made a motion for the P&T Committee to resume the meeting in another room to discuss this confidential information regarding prices charged by the manufacturers and wholesalers of the drug classes

discussed at this P&T Committee meeting. This confidential meeting is authorized by Federal Law at 42 U.S.C. § 1396r-8(b) (3) (D) that requires this information to be kept confidential.

This motion was seconded and unanimously approved by the Committee.

The meeting adjourned to an executive session.

The Committee returned to the room.

Mark Oley confirmed that to the best of each of the Committee members' knowledge the only information discussed at the confidential meeting was information regarding prices charged by the manufacturers and wholesalers of the drug classes discussed at this P&T Committee meeting. As authorized by Federal Law at 42 U.S.C. § 1396r-8(b) (3) (D) that requires this information to be kept confidential.

Mark Oley made a motion for the Committee to resume the meeting to discuss the PDL .
The motion was seconded to resume the meeting.
The committee voted unanimously to resume the meeting to discuss the PDL.

Criteria Discussion of Phase II New Drugs

A motion was made to retain the PDL for CNS Stimulants /ADHD with no change (making the new drug, Daytrana®, non-preferred).
The motion was seconded.
The Committee voted unanimously to leave as the current PDL CNS Stimulants /ADHD with no change.

A motion was made to add the generic Macrolides, azithromycin and clarithromycin, to the PDL as preferred.
The motion was seconded
The Committee voted unanimously to add the generic Macrolides, azithromycin and clarithromycin, to the PDL as preferred.

A motion was made to add the generic Ophthalmic Antihistamines, ketotifen fumerate, to the PDL as preferred.
The motion was seconded.
The Committee voted unanimously to add the generic Ophthalmic Antihistamines, ketotifen fumerate, to the PDL as preferred.

Criteria Discussions for PDL Phase I Drug Classes

Mark Oley reviewed recommendations for preferred drugs in the HMG CoA Reductase Inhibitors (Statins) class as:
Advicor ®
Altoprev ®
Lescol ®
Lescol XL ®
Lovastatin
Pravachol ®
Simvastatin
Zetia ®

The motion was made to remove Zocor® and add simvastatin as preferred for this drug class.

This motion was seconded and unanimously approved by the Committee.

Mark Oley noted that no change was recommended in the Lipotropics Non-Statins: Fibric Acid class.
A motion was made to accept as read by Mark Oley.
This motion was seconded and unanimously approved by the Committee.

Mark Oley noted that no change was recommended in the Lipotropics Non-Statins: Niacin Derivatives class.
A motion was made to accept as read by Mark Oley.
This motion was seconded and unanimously approved by the Committee.

Mark Oley noted that no change was recommended in the Angiotensin Receptor Blockers (and ARB combinations) class.
A motion was made to accept as read by Mark Oley.
This motion was seconded and unanimously approved by the Committee

Mark Oley noted that no change was recommended in the Angiotensin Converting Enzyme Inhibitors (and ACE Inhibitors combos) class.
A motion was made to accept as read by Mark Oley.
This motion was seconded and unanimously approved by the Committee.

Mark Oley noted that no change was recommended in the Beta Blockers class.
A motion was made to accept as read by Mark Oley.
This motion was seconded and unanimously approved by the Committee.

Mark Oley noted that no change was recommended in the Calcium Channel Blockers class.
A motion was made to accept as read by Mark Oley.
This motion was seconded and unanimously approved by the Committee.

Mark Oley noted that no change was recommended in the Phosphodiesterase 5 Inhibitor for Pulmonary Arterial Hypertension class.
A motion was made to accept as read by Mark Oley.
This motion was seconded and unanimously approved by the Committee.

Mark Oley reviewed recommendations for preferred drugs in the Inhaled Corticosteroids class as:
Advair Diskus ®
Advair HFA ®
Aerobid ®
Aerobid-M ®
Asmanex ®
Azmacort ®
Flovent HFA ®
Pulmicort Respules®
QVAR ®

A motion was made to accept as read by Mark Oley.
This motion was seconded and unanimously approved by the Committee.

Mark Oley noted that that no change was recommended in the Nasal Steroids class.
A motion was made to accept as read by Mark Oley.
This motion was seconded and unanimously approved by the Committee.

Mark Oley noted that that no change was recommended in the in the Beta Adrenergics class.
A motion was made to accept as read by Mark Oley.
This motion was seconded and unanimously approved by the Committee.

Mark Oley noted that that no change was recommended in the COPD-Anticholinergics class.
A motion was made to accept as read by Mark Oley.
This motion was seconded and unanimously approved by the Committee.

Mark Oley noted that no change was recommended in the Second Generation Antihistamines (LSAs) class.
A motion was made to accept as read by Mark Oley.
This motion was seconded and unanimously approved by the Committee.

Mark Oley noted that no change was recommended in the H2 Antagonists class.
A motion was made to accept as read by Mark Oley.
This motion was seconded and unanimously approved by the Committee.

Mark Oley noted that no change was recommended in the Benzodiazepine Sedative Hypnotics class.
A motion was made to accept as read by Mark Oley.
This motion was seconded and unanimously approved by the Committee.

Mark Oley recommended that Rozerem® be added as a preferred drug in the Other Sedative Hypnotics class.

Dr. Axelrod noted that Committee already made a change in the criteria for over age 65. The Committee discussed the criteria in people under 65 years of age.
Mark Oley made the motion for a step edit for the less than 65 years of age population with the first step being a generic and second step Rozerem®.
This motion was seconded and unanimously approved by the Committee

Mark Oley noted that no change was recommended in the Electrolyte Depleters class.
A motion was made to accept as read by Mark Oley.
This motion was seconded and unanimously approved by the Committee.

Mark Oley noted that no change was recommended in the Urinary Tract Antispasmodics class.
A motion was made to accept as read by Mark Oley.
This motion was seconded and unanimously approved by the Committee.

Mark Oley noted that no change was recommended in the Cox-2 Inhibitors class.
A motion was made to accept as read by Mark Oley.
This motion was seconded and unanimously approved by the Committee.

Mark Oley noted that no change was recommended in the Topical Immunomodulators class.
A motion was made to accept as read by Mark Oley.
This motion was seconded and unanimously approved by the Committee.

Mark Oley noted that no change was recommended to the preferred status of drugs in the Proton Pump Inhibitors (PPIs) class. Prilosec® OTC and Protonix ® will continue to be preferred. The Committee discussed the components of the step edit and the duration of therapy for this class.

A motion was made for the step edit in the PPI class to be defined as follows:

- Prilosec® OTC and Protonix® are the preferred products on the PDL with step edits.
- Step 1 requires a therapeutic failure of a 60-day trial of OTC Prilosec® (up to 40mg daily).

- Exceptions are people over 65 years of age or with a diagnosis of:
  - Active GI Bleed
  - Erosive Esophagitis
  - Zollinger-Ellison Syndrome

Duration of therapy for treatment with a PPI is recommended for 120 days unless one of the following is met:

- Erosive Esophagitis
- Active GI Bleed
- Zollinger-Ellison
- Greater than 65 years of age
- Is under the care of a Gastroenterologist, or has undergone a scope procedure to rule out a nonsecretory condition.

A motion was made to accept the recommendations as stated.
This motion was seconded and unanimously approved by the Committee

A clarification was made that if one of the above is met, then therapy to be approved for 1 year.

A presentation on the standard of care for the PPI class was requested for the next meeting.

The next meeting of the P&T Committee will be scheduled for Spring 2007.

The meeting was adjourned.